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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/055,143	01/22/2002	John Chapman	18242-508 CIP2 (VI-8 CIP2	1572

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EXAMINER	
SNYDER, STUART	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 08/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/055,143	CHAPMAN ET AL.	
	Examiner	Art Unit	
	Stuart W. Snyder	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 July 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *6-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,13-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Amendment filed July 5, 2006 in response to the Office Action of April 5, 2006 is acknowledged and has been entered. Claims 1-5 and 13-20 are pending and are currently being examined. Claims 6-12 were previously withdrawn.

The text of those sections of Title 35, US Code not included in this action can be found in a prior Office Action.

Claim Rejections - 35 USC § 102

Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Meryman *et al.* (WO 91/04659) as previously stated in the Office Action mailed 4/5/2006. The instant invention is drawn to reducing the amount of an analyte found in mammalian blood. Removal of the extra-cellular fluid from a red blood cell suspension results in a reduction of an analyte present in the extra-cellular fluid.

Applicant has twice traversed the rejection and twice amended claim 1 to overcome the rejection. Claim 1 as amended requires that (a) the wash solution contain chloride, and (b) that the concentration of DPG in the blood cell suspension falls to greater than or equal to approximately half of its initial concentration at 21 days.

Applicants' arguments have been fully considered but fail to persuade. Applicants' arguments are summarized:

1. Although some of the wash solutions taught in Meryman contained chloride, as a rule they seemed to result in poorer storage results regardless of storage solution.

2. A correlate of red blood cell function is the concentration of DPG in the blood cell suspension and high levels are maintained when the wash solution contains chloride in the instant invention.

Applicants' arguments are unpersuasive because they fail to account for the critical factors described in Meryman *et al.* and references therein, specifically the maintenance of intracellular pH and the osmolarity of the wash and storage solutions. Applicant uses "normal saline" which is isotonic with respect to chloride ions in human blood and hence the intracellular chloride concentrations. Meryman used hypotonic solutions without membrane permeable anions—including chloride--for washing and storing to swell the erythrocytes during storage resulting increased shelf life of the RBCs. Only in the hypotonic condition with permeable anions does the chloride effect of decreased RBC viability manifest itself. Specific teaching about using chloride containing wash buffers are found Meryman *et al.*'s description—see especially page 4, lines 4-6 and page 5, line 5—for the delineated purposes of removal of unwanted small molecules, viruses and viricidal agents. It is the osmotic character of the wash buffer combined with the presence or absence of membrane permeable anions that influence the effect of the wash buffer. Thus the amended claims, having inclusion of limitations drawn toward both chloride wash solutions and maintenance of DPG, are irrelevant in overcoming the anticipation rejection and applicants' arguments are unconvincing. The rejection of claims 1 and 2 under 35 USC 102(b) is proper and the rejections are maintained for reasons of record.

Claim Rejections - 35 USC § 103

Claims 1-5 and 13-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meryman *et al.* (WO 91/04659) in view of Edson *et al.* (WO 00/18969) as previously stated in the Office Action mailed 4/5/2006.

Applicants' traverse the rejection based on the amendment of claim 1 to include a recitation of maintenance of a certain DPG concentration at day 21 of storage. Applicants correctly point out that DPG is a correlate of RBC functional viability and, as such, would be an inherent characteristic of any procedure that maintained RBC viability.

In response and as noted above, applicant fails to consider the effect of osmolarity in the washing conditions. Applicants' assertion that maintaining DPG levels at or above 50% after 21 days of storage despite being washed in a wash solution containing chlorine is an unexpected result is false. Chloride-containing buffers used in the instant application were isotonic. In contrast, the buffers used by Meryman, *et al.* are hypotonic with respect to non-permeable ions. One might reasonably expect for the presence of chloride to have an effect in hypotonic conditions. Indeed, part of the motivation for investigating the effect of chloride effect in hypotonic conditions was Meryman *et al.*'s previous work in which wash and storage solutions containing ammonium chloride resulted in red blood cells with high levels of ATP and DPG after 21 and 42 day of 4° C (Meryman HT, Hornblower ML, Syring RL. "Prolonged storage of red cells at 4 degrees C"

Transfusion. 1986 Nov-Dec;26(6):500-5.). Thus, applicants' observation of chloride presence in the wash not having a negative effect on the subsequent storage of RBCs does not constitute an unexpected result but rather results that would be expected under the experimental conditions. Therefore, rejection of claims 1-5 and 13-20 under 35 USC 103(b) as being obvious over Meryman in view of Edson are maintained.

Claims 1-5 and 13-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meryman *et al.* and Edson *et al.* (WO 00/18969) in light of Sharma (US Patent No. 6,234,239) as previously stated in the Office Action mailed 4/5/2006.

The Office asserted that Sharma teaches a method of washing RBCs with a sterile phosphate buffered saline solution and storing the cells for 20 days in a refrigerator. Applicants argue that Sharma does not remedy the deficiencies of Meryman and Edson because it does not specifically teach the DPG levels of the RBCs nor does it teach any correlates of RBC viability from which DPG levels can be inferred. Applicant continues with the assertion that antiviral treatment, washing with a saline-containing wash buffer, and subsequent storage of cells in a storage buffer for up to 39 day at 4° C results in loss of RBC count, hemoglobin and hematocrit specifically pointing to the data of Tables IX and X of Sharma.

The arguments of applicant have been considered and are unconvincing. Concerning correlates of RBC viability and usefulness for transfusion: Applicant cites, among other attributes correlated with the usefulness of stored RBCS, biological, morphological and extent of lysis. However, shelf-life of RBCs are

determined on the basis of the percentage of circulating RBCs after transfusion which is a direct function of the morphology of the cells but is indirectly associated with the ATP and GCP levels. In contrast to the assertations of applicant to the contrary, Sharma convincingly demonstrates no significant change in morphology when treating, washing and storing RBCs for up to 39 days. Although the Sharma data that applicant cites relate to treatment of whole blood, there is no significant difference between control values and test object values:

TABLE IX

Hematological data on packed cells prepared from whole blood treated with the composition in vitro.

	Control	Composition(%) in blood over 1 hour treatment		
Parameter	0.0	0.5	1.0	2.0
Leukocytes x 10^3/cmm	5.0	5.1	5.2	5.2
Erythrocytes x 10^6/cmm	3.5	3.4	3.3	3.3
Hemoglobin g/DL	13.5	13.8	13.7	13.6
Hematocrit %	38.5	37.6	39.1	38.5
MCV cu micron	108.0	108.0	108.0	109.0
Red cell deformability Ectacytometry (290 nm)*	0.565	0.585	0.585	0.590

*after 20 days of storage in the refrigerator.

TABLE X

Hematological Tests on Composition Treated Blood Stored in Adsol for 39 Days in Refrigerator

	Tests for red cell stability			
Treatment of Blood (1 hr)	Ectacytometer stress test (290 nm)	RBC x (million/ml)	HgB GMS/DL	HCT (%)
Untreated control	0.545	3.40	11.8	36.1
Composition				
0.5%	0.535	3.36	11.6	35.1
1.0%	0.545	3.36	11.8	35.6
2.0%	0.535	3.37	11.9	35.9

Notice that the variation between control and any of the test values is less than 2% and often less than 1% that is well within the standard errors associated with any of theses tests. Furthermore, Sharma teaches that treatment, washing with saline solutions and subsequent storage for up to 19 days did not result in RBC morphological changes—see especially Sharma column 10, line 45; column 14, line 47. Applicants' argument that Sharma doesn't teach retention of RBC viability after washing with saline solution after virucidal treatment and subsequent storage is erroneous and rejected. Therefore, rejection of claims 1-5 and 13-20 under 35 USC 103(b) as being obvious over Meryman and Edson in view of Sharma are maintained.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PRO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989). The Group 1600 Official Fax number is: (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Tech Center representative whose telephone number is (571)-872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart W. Snyder whose telephone number is (571) 272-9945. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce R. Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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